

wherein

R^1 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, hydroxy, alkoxy, C-carboxy, O-carboxy, acetyl, C-amido, C-thioamido, sulfonyl and trihalomethanesulfonyl;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl and heteroalicyclic;

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R^3 , R^4 , R^5 and R^6 are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, trihalomethane-sulfonamido, carbonyl, C-carboxy, O-carboxy, C-amido, N-amido, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, amino and $-NR^{11}R^{12}$;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, carbonyl, acetyl, sulfonyl, trifluoromethanesulfonyl and, combined, a five- or six-member heteroalicyclic ring;

R^3 and R^4 , R^4 and R^5 , or R^5 and R^6 may combine to form a six-member aryl ring, a methylenedioxy group or an ethylenedioxy group;

R^7 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, carbonyl, acetyl, C-amido, C-thioamido, amidino, C-carboxy, O-carboxy, sulfonyl and trihalomethane-sulfonyl;

R^9 is $-(alk_1)Z$, wherein Alk_1 is selected from the group consisting of alkyl, alkenyl or alkynyl, and Z is a polar group;

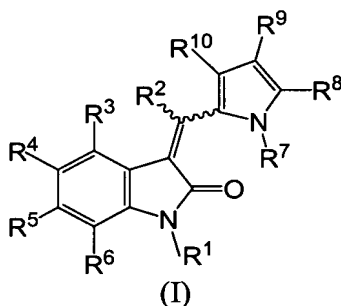
R^8 and R^{10} are independently selected from hydrogen and unsubstituted lower alkyl;

one or more polyoxyhydrocarbyl compounds; and

a pharmaceutically acceptable carrier therefor;

wherein said ionizable substituted indolinone is solubilized by combining said indolinone with a molar equivalent of a base solution or an acid solution.

76. (Twice amended) A method of making a formulation suitable for oral administration comprising admixing an ionizable substituted indolinone of Formula (I):



wherein

R^1 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, hydroxy, alkoxy, C-carboxy, O-carboxy, acetyl, C-amido, C-thioamido, sulfonyl and trihalomethanesulfonyl;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl and heteroalicyclic;

R^3 , R^4 , R^5 and R^6 are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, trihalomethane-sulfonamido, carbonyl, C-carboxy, O-carboxy, C-amido, N-

amido, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, amino and $-NR^{11}R^{12}$;

R^{11} and R^{12} are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, carbonyl, acetyl, sulfonyl, trifluoromethanesulfonyl and, combined, a five- or six-member heteroalicyclic ring;

R^3 and R^4 , R^4 and R^5 , or R^5 and R^6 may combine to form a six-member aryl ring, a methylenedioxy group or an ethylenedioxy group;

R^7 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, carbonyl, acetyl, C-amido, C-thioamido, amidino, C-carboxy, O-carboxy, sulfonyl and trihalomethane-sulfonyl;

R^9 is $-(alk_1)Z$, wherein Alk_1 is selected from the group consisting of alkyl, alkenyl or alkynyl, and Z is a polar group;

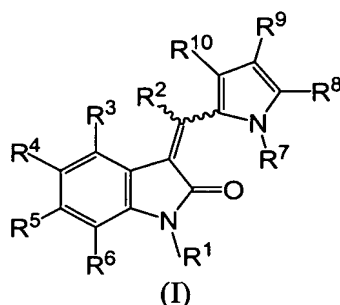
R^8 and R^{10} are independently selected from hydrogen and unsubstituted lower alkyl;

one or more pharmaceutically acceptable surfactants; and

one or more pharmaceutically acceptable oils.

78. (Twice amended) A method of treating a protein kinase related disorder in a patient in need of treatment comprising:

a) diluting a parenteral formulation into a pharmaceutically acceptable solution, said parenteral formulation comprising an ionizable substituted indolinone of Formula (I):



wherein

R^1 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, hydroxy, alkoxy, C-carboxy, O-carboxy, acetyl, C-amido, C-thioamido, sulfonyl and trihalomethanesulfonyl;

R^2 is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl and heteroalicyclic;

R^3 , R^4 , R^5 and R^6 are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, trihalomethane-sulfonamido, carbonyl, C-carboxy, O-carboxy, C-amido, N-amido, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, amino and $-NR^{11}R^{12}$;

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 R^{11} and R^{12} are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, carbonyl, acetyl, sulfonyl, trifluoromethanesulfonyl and, combined, a five- or six-member heteroalicyclic ring;

R^3 and R^4 , R^4 and R^5 , or R^5 and R^6 may combine to form a six-member aryl ring, a methylenedioxy group or an ethylenedioxy group;

R^7 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, carbonyl, acetyl, C-amido, C-thioamido, amidino, C-carboxy, O-carboxy, sulfonyl and trihalomethane-sulfonyl;

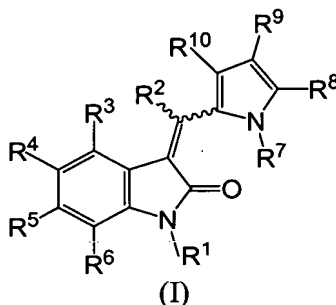
R^9 is $-(alk_1)Z$, wherein Alk_1 is selected from the group consisting of alkyl, alkenyl or alkynyl, and Z is a polar group;

R^8 and R^{10} are independently selected from hydrogen and unsubstituted lower alkyl, one or more polyoxyhydrocarbyl compounds and

a buffer; and

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b) parenterally administering said diluted formulation to said patient.

80. (Twice amended) A method of treating a protein kinase related disorder in a patient in need of treatment comprising orally administering to said patient a formulation comprising an ionizable substituted indolinone of Formula (I):



wherein

B⁴
R¹ is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, hydroxy, alkoxy, C-carboxy, O-carboxy, acetyl, C-amido, C-thioamido, sulfonyl and trihalomethanesulfonyl;

R² is selected from the group consisting of hydrogen, halo, alkyl, cycloalkyl, aryl, heteroaryl and heteroalicyclic;

R³, R⁴, R⁵ and R⁶ are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, mercapto, alkylthio, arylthio, sulfinyl, sulfonyl, S-sulfonamido, N-sulfonamido, trihalomethane-sulfonamido, carbonyl, C-carboxy, O-carboxy, C-amido, N-amido, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, amino and -NR¹¹R¹²;

R¹¹ and R¹² are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, carbonyl, acetyl, sulfonyl, trifluoromethanesulfonyl and, combined, a five- or six-member heteroalicyclic ring;